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L2: Entry 8 of 8 File: USPT Jan 21, 1997

US-PAT-NO: 5595885
DOCUMENT-IDENTIFIER: US 5595885 A

TITLE: Matrix metalloproteinase inhibitor peptides

DATE-ISSUED: January 21, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Stetler-Stevenson; William G.	Gaithersburg	MD		
Liotta; Lance A.	Potomac	MD		
Krutzsch; Henry C.	Bethesda	MD		

US-CL-CURRENT: 435/69.2; 435/252.3, 536/23.1, 536/23.5, 536/25.3

CLAIMS:

What is claimed is:

1. An isolated nucleic acid having a sequence which encodes the 194 amino acid polypeptide of FIG. 8.

2. An isolated nucleic acid of claim 1 having a sequence of FIG. 7.

3. An isolated nucleic acid of claim 1, wherein a promoter is operably linked to the nucleic acid.

4. An isolated nucleic acid of claim 3, wherein the promoter and the nucleic acid are contained in an expression vector.

5. A cell transformed or transfected with a nucleic acid of claim 1.

6. A cell transformed or transfected with a nucleic acid of claim 4.

7. A method of producing the 194 amino acid polypeptide of FIG. 8 by introducing into a suitable host cell an expression vector having a promoter operably linked to a nucleic acid which encodes said polypeptide and recovering said polypeptide from said cell.

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Krutzsch; Henry C.	Bethesda	MD		

ASSIGNEE-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY	TYPE CODE
The United States of America as represented by the Department of Health	Washington	DC			06

APPL-NO: 08/ 039525 [PALM]
DATE FILED: March 29, 1993

PARENT-CASE:
This application is a continuation of application Ser. No. 07/494,796, filed Mar. 13, 1990, now abandoned, which is a continuation-in-part of application Ser. No. 07/395,453, filed Aug. 18, 1989, now abandoned, which is a continuation-in-part of application Ser. No. 07/380,431, filed Jul. 17, 1989, which is a continuation-in-part of application Ser. No. 07/326,334, filed Mar. 21, 1989, now abandoned.

INT-CL: [06] C12 N 15/00

US-CL-ISSUED: 435/69.2; 435/172.3, 435/252.3, 536/23.1, 536/23.5, 536/25.3
US-CL-CURRENT: 435/69.2; 435/252.3, 536/23.1, 536/23.5, 536/25.3

FIELD-OF-SEARCH: 435/6, 435/69.2, 435/172.3, 435/320.1, 435/252.3, 435/240.1, 536/23.1, 536/23.5, 536/25.3

PRIOR-ART-DISCLOSED:

OTHER PUBLICATIONS

Docherty et al "Sequence of human tissue inhibitor of metalloproteinases" Nature vol. 318, pp. 66-69. 7 Nov. 1985.

ART-UNIT: 183

PRIMARY-EXAMINER: Nucker; Christine M.

ASSISTANT-EXAMINER: Scheiner; Laurie

ABSTRACT:

The present invention is an isolated protein of 21,600 Da which binds to both latent and activated type IV collagenase with high affinity at 1:1 molar stoichiometry, thereby abolishing enzyme activity. The protein is purified by affinity chromatography on solid phase metalloproteinase, or solid phase metalloproteinase substrates which bind the enzyme-inhibitor complex. The complete primary structure of this protein (initially called CSC-21K), as determined by sequencing overlapping peptides spanning the entire protein, reveals homology with a protein called TIMP, Tissue Inhibitor of Metalloproteinases. In addition, a cDNA for this novel inhibitor, now designated TIMP-2, was cloned from a melanoma cell and its sequence was compared with that of human TIMP-1. Northern blots of melanoma cell mRNA showed two distinct transcripts of 0.9 kb and 3.5 kb which are down-regulated by transforming growth factor-.beta., and are unchanged by phorbol ester treatment. The inhibitor of the present invention may be used for treatment of pathologic conditions resulting from inappropriate degradation of extracellular matrix molecules by matrix metalloproteinases, such as metastatic neoplasia, myocardial infarction, and arthritis. Therapeutic treatments using this inhibitor may include formulations for inhalation and inclusion complexes adapted for buccal or sublingual administration, or administration of a recombinant DNA molecule which expresses a DNA segment that encodes the matrix metalloproteinase inhibitor of this invention.

7 Claims, 14 Drawing figures